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(54) Title: G PROTEIN-COUPLED RECEPTORS

(57) Abstract: The present invention provides a gene encoding a G protein-coupled receptor termed nGPCR-x; constructs and recombinant host cells incorporating the genes; the nGPCR-x polypeptides encoded by the gene; antibodies to the nGPCR-x polypeptides; and methods of making and using all of the foregoing.

# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/US 00/35456

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C07K14/72 C12N15/12 C12N15/861 C12N15/863 C12N15/864  
 C12N15/867 C12N15/869 C12N5/10 C07K16/28 G01N33/53  
 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N C07K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

GENSEQ, EPO-Internal, WPI Data, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No.  |
|----------|---|--|
| X        | <p>DATABASE GENEMBL 'Online!<br/>13 July 1997 (1997-07-13)<br/>TRENKLE ET AL.: "AF003828 human<br/>erythroleukemia RAP-PCR products Homo<br/>sapiens cDNA clone TF-1/A1-1, mRNA<br/>sequence"<br/>XP002170928</p> <p>Accession AF003828</p> <p>---</p> <p>-/-</p> | <p>1-4, 7-9,<br/>12-27,<br/>29-34,<br/>40, 44,<br/>45, 47,<br/>48, 50,<br/>51, 53,<br/>58-60</p> |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

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## II INTERNATIONAL SEARCH REPORT

|                              |
|------------------------------|
| International Application No |
| PCT/US 00/35456              |

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.  |
|------------|--|--|
| X          | WO 98 46620 A (MILLENNIUM PHARM INC)<br>22 October 1998 (1998-10-22)<br><br>page 4, line 19 -page 7, line 3<br>page 28, line 6 -page 45, line 4<br>page 55, line 6 -page 62, line 14<br>---  | 1-5,<br>7-10,<br>12-27,<br>29-38,<br>40-45,<br>47-53,<br>55-60,<br>86-88                               |
| A          | WO 99 32519 A (FORTIN YVES ;LEMBO PAOLA (CA); AHMAD SULTAN (CA); BANVILLE DENIS ()<br>1 July 1999 (1999-07-01)<br>page 1, line 25 -page 5, line 20<br>figures 1,4; examples 1,2<br>SEQ ID NO: 3,7,9<br>---   | 1-62,<br>64-89   |
| P, X       | WO 00 34334 A (SYNAPTIC PHARMA CORP)<br>15 June 2000 (2000-06-15)<br><br>page 3 -page 14<br>---  | 1-5,<br>7-10,<br>12-27,<br>29-38,<br>40-45,<br>47-53,<br>55-60,<br>86-88                               |
| E          | WO 01 19983 A (DELEERSNIJDER WILLY ;HEUVAERT NICOLE D (BE); NYS GUY (BE);<br>SOLVAY) 22 March 2001 (2001-03-22)<br><br>page 11 -page 29<br>---   | 1-5,<br>7-10,<br>12-27,<br>29-38,<br>40,44,<br>45,47,<br>48,50,<br>51,53,<br>55,56,<br>58-60,<br>86-88 |
| E          | WO 01 18206 A (LEXICON GENETICS INC)<br>15 March 2001 (2001-03-15)<br>page 6, line 23 -page 7, line 25<br>page 10, line 31 -page 11, line 3<br>page 11, line 29 -page 12, line 7<br>page 13, line 25 -page 14, line 14<br>page 14, line 23 -page 24, line 17<br>page 26, line 7 -page 29, line 3<br>page 39, line 1 -page 57, last line<br>--- | 1-60,<br>73-86,89  |
|            |  | -/-  |

## II INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/35456

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |  |  |
|--|--|--|
| Category *   | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.  |
| E  | <p>DATABASE WPI<br/>Section Ch, Week 200123<br/>Derwent Publications Ltd., London, GB;<br/>Class B04, AN 2001-226684<br/>XP002183350<br/>&amp; WO 01 16309 A (TAKEDA CHEM IND LTD),<br/>8 March 2001 (2001-03-08)</p> <p>abstract<br/>-&amp; DATABASE GENSEQ 'Online!<br/>29 May 2001 (2001-05-29)<br/>WATANABE, T. ET AL.: "Human<br/>G-protein-coupled receptor protein"<br/>XP002183348<br/>Accessions AAB70143<br/>-&amp; DATABASE GENSEQ 'Online!<br/>29 May 2001 (2001-05-29)<br/>WATANABE, T. ET AL.: "DNA encoding human<br/>G-protein-coupled receptor protein"<br/>XP002183349<br/>Accession AAF79502<br/>----</p> <p>WO 01 62797 A (PARODI LUIS A ;LIND PETER<br/>(SE); UPJOHN CO (US); VOGELI GABRIEL (US)<br/>30 August 2001 (2001-08-30)<br/>see claims<br/>SEQ ID NO:53,113<br/>----</p> <p>WO 01 72840 A (PE CORP NY)<br/>4 October 2001 (2001-10-04)<br/>page 6, last paragraph -page 44<br/>SEQ ID NOs:3,4<br/>-----</p> | 1-5,<br>7-10,<br>12-27,<br>29-38,<br>40-45,<br>47-53,<br>55-60,<br>86-88 |
| E  |  | 1-62,<br>64-89   |
| E  |  | 1-62,<br>64-89   |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/35456

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim 44 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: 41-43, 49, 52, 57 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 41-43, 49,52,57

Present claims 41-43 relate to an antibody defined by reference to a desirable characteristic or property, namely, its ability to bind the polynucleotide of the invention. The claims cover all antibodies having this characteristic or property, whereas the application provides neither support within the meaning of Article 6 PCT nor disclosure within the meaning of Article 5 PCT for none of such antibodies. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the antibody by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried out for those claims.

Present claims 49,52,57 relate to compounds defined by reference to a desirable characteristic or property, namely, their ability to be identified by the methods of claims 45, 50 and 53, respectively. The claims cover all compounds having this characteristic or property, whereas the application provides neither support within the meaning of Article 6 PCT nor disclosure within the meaning of Article 5 PCT for none of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-5, 7-10, 12-27, 29-38, 40-45, 47-53, 55-60 and 86-88 (partially)

An isolated nucleic acid molecule (SEQ ID NO:11) encoding a polypeptide comprising an aminoacid sequence (SEQ ID NO:24) coding for the G-protein coupled receptor nGPCR-1003; expression vector and host cells containing said polynucleotide, a method for the recombinant production of the polypeptide of the invention; an antibody that binds to the polypeptide of the invention; methods to identify compounds that bind to the nGPCR-1003 polynucleotide or nGPCR-1003 polypeptide; a method of identifying an animal homolog of nGPCR-1000; a method to purify a G-protein from a sample by binding to nGPCR-1000.

2. Claims: 1-61, 64-86, 89 (partially) and 63 (complete).

As invention 1, but referring to the G-protein coupled receptor nGPCR-1007 (SEQ ID NOs: 25) encoded by the polynucleotide of SEQ ID NO: 12; in addition, the invention also claims methods to diagnose a brain disorder or a genetic predisposition to a mental disorder and by detecting mutations in nGPCR-1007; kits for carrying out above methods; a method for identifying a nGPCR-1007 allelic variant; a method for identifying a modulator of biological activity of nGPCR-1007; a method to identify compounds useful in the treatment of a mental disorder by identifying compounds which bind to nGPCR-1007.

3. Claims: 1-5, 7-10, 12-27, 29-38, 40-45, 47-53, 55-60 and 86-88 (partially)

As invention 1, but referring to the G-protein coupled receptor nGPCR-1006 (SEQ ID NOs: 26,27) encoded by the polynucleotide of SEQ ID NO: 13.

4. Claims: 1-61, 64-89 (partially) and 62 (complete).

As invention 1, but referring to the G-protein coupled receptor nGPCR-1002 (SEQ ID NO: 46) encoded by the polynucleotide of SEQ ID NO: 45; in addition, the invention also claims methods to diagnose a brain disorder or a genetic predisposition to a mental disorder and by detecting mutations in nGPCR-1002; kits for carrying out above methods; a method for identifying a nGPCR-1002 allelic variant; a method for identifying a modulator of biological activity of nGPCR-1002; a method to identify compounds

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

useful in the treatment of a mental disorder by identifying compounds which bind to nGPCR-1002.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-5, 7-10, 12-27, 29-38, 40-45, 47-53, 55-60 and 86-88 (partially)

An isolated nucleic acid molecule (SEQ ID NO:11) encoding a polypeptide comprising an aminoacid sequence (SEQ ID NO:24) coding for the G-protein coupled receptor nGPCR-1003; expression vector and host cells containing said polynucleotide, a method for the recombinant production of the polypeptide of the invention; an antibody that binds to the polypeptide of the invention; methods to identify compounds that bind to the nGPCR-1003 polynucleotide or nGPCR-1003 polypeptide; a method of identifying an animal homolog of nGPCR-1000; a method to purify a G-protein from a sample by binding to nGPCR-1000.

2. Claims: 1-61, 64-86, 89 (partially) and 63 (complete).

As invention 1, but referring to the G-protein coupled receptor nGPCR-1007 (SEQ ID NOs: 25) encoded by the polynucleotide of SEQ ID NO: 12; in addition, the invention also claims methods to diagnose a brain disorder or a genetic predisposition to a mental disorder and by detecting mutations in nGPCR-1007; kits for carrying out above methods; a method for identifying a nGPCR-1007 allelic variant; a method for identifying a modulator of biological activity of nGPCR-1007; a method to identify compounds useful in the treatment of a mental disorder by identifying compounds which bind to nGPCR-1007.

3. Claims: 1-5, 7-10, 12-27, 29-38, 40-45, 47-53, 55-60 and 86-88 (partially)

As invention 1, but referring to the G-protein coupled receptor nGPCR-1006 (SEQ ID NOs: 26,27) encoded by the polynucleotide of SEQ ID NO: 13.

4. Claims: 1-61, 64-89 (partially) and 62 (complete).

As invention 1, but referring to the G-protein coupled receptor nGPCR-1002 (SEQ ID NO: 46) encoded by the polynucleotide of SEQ ID NO: 45; in addition, the invention also claims methods to diagnose a brain disorder or a genetic predisposition to a mental disorder and by detecting mutations in nGPCR-1002; kits for carrying out above methods; a method for identifying a nGPCR-1002 allelic variant; a method for identifying a modulator of biological activity of nGPCR-1002; a method to identify compounds

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

useful in the treatment of a mental disorder by identifying compounds which bind to nGPCR-1002.

## II INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/US 00/35456

| Patent document cited in search report | Publication date | Patent family member(s) |  | Publication date |
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